REMARKS

Claims 1-6 and 8-15 were pending in the present application prior to entry of the present amendment. By virtue of this response, claim 6 and claims 11-15 have been cancelled, without prejudice; claim 1 has been amended to recite human and to recite, in part, wherein an adjuvant is not administered in conjunction with administration of said composition; and new claims 16-17 have been added. Support for the amendment to claim 1 can be found at least at page 13, lines 5-10 and at page 32, lines 8-10. Support for new claim 16 can be found at least at page 20, lines 18-24. Support for new claim 17 can be found at least at page 32, lines 8-10. Accordingly, claims 1-5, 8-10 and 16-17 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented. Applicant reserves the right to prosecute the subject matter of cancelled and amended claims in related applications.

MPEP 707.02

This application was filed March 9, 2001 and therefore has been pending five years. The instant office action is the 8th Office Action (including the Advisory Action) mailed by the USPTO in the file history. The instant Office Action is the 3rd non-final Office Action since the RCE was filed January 9, 2004.

MPEP 707.02[1] states that any application that has been pending five years should be carefully studied by the supervisory patent examiner and every effort should be made to terminate its prosecution. Pursuant to MPEP 707.02, Applicants request that the Supervisory examiner, James Housel, review this application with a view to finally concluding its prosecution. MPEP 707.02 states that to accomplish this result, the application is to be considered "special" by the examiner. Applicants request that the examiner consider this application as "special" due to the length of its pendency and the number of Office Actions mailed.

[1] Applications up for third action and 5-year applications.

Rejection of Claims Under 35 U.S.C. 112, First Paragraph

Claims 1-6, and 8-15 stand rejected under 35 U.S.C., first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner indicates that this is a new ground of rejection that does not concern the size range of the ISS claimed. See the Office Action at page 8.

Applicant traverses this rejection. To comply with the requirements of Section 112, first paragraph, enablement, a specification must adequately teach how to make and how to use the claimed invention, throughout its scope without undue experimentation. Those of skill in the art at the time of the filing would understand how to make and use the claimed invention without undue experimentation.

At page 3 of the Office Action, the Examiner alleges that regarding the administration of ISS without RSV antigen, the state of the art at the time the application was filed provided that an ISS could be administered as an adjuvant[2] to increase vaccine efficacy. The Examiner also alleges at page 3 that the "paradigm held that an immune response against a specific pathogen at least required the recognition of antigen". While these allegations are unsupported by any references, the Examiner's understanding of the state of the art supports the non-obviousness of the claimed invention. Whether or not the Examiner's characterization of the state of the art is correct, the instant application *demonstrates* that in the animal model described in the Examples, intranasal administration of an ISS without administration of an RSV antigen, an immunostimulatory cytokine and an adjuvant results in a reduction in RSV viral titer. Furthermore, the "state of the art" factor alone, whether the Examiner's characterization of it is correct or flawed, is not enough to support a finding of non-enablement.

The Examiner relies on Kobayashi et al. in alleging at page 3 of the Office Action that the ability of increased Th1 activity[3] to impact infection depends on the presence of a disease

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[2] Webster's Ninth New Collegiate Dictionary (Merriam-Webster Inc., Publishers, Springfield, Massachusetts) defines adjuvant as an ingredient that modifies the action of the principal ingredient (attached as Exhibit A).

[3] The Examiner acknowledges that it was known that ISS were capable of increasing Th1 activity.

specific antigen. The Examiner alleges that the activity of Th1 cells is modulated by antigen/MHC complexes on the surface of target macrophage cells. The Examiner then alleges that without co-administration of an antigen, one skilled in the art could not predict how an ISS alone could impact infection. The standard for compliance with Section 112, first paragraph enablement is that a specification must adequately teach how to make and how to use the claimed invention, throughout its scope without undue experimentation. The standard is not whether one of skill in the art would predict an outcome. The instant specification provides disclosure as to how to make and use the invention across its full scope and *demonstrates* that in the animal model and conditions provided in the examples, administration of an ISS without co-administration of an RSV antigen, an immunostimulatory cytokine and an adjuvant results in a reduction in RSV viral titer. It appears that the Examiner has inappropriately dismissed the teachings of the specification, and has not provided acceptable documentation or sound scientific reasoning to support any doubt of the teachings of the specification. See, for example, In re Marzocchi, 439, F2nd 220, 224, 169 USPQ 367,370 (CCPA 1071). Applicants submit that no *prima facie* case of non-enablement has been made based on the Kobayashi disclosure.

The Examiner alleges that there is no teaching or working example of suppressing infection. While compliance with Section 112, first paragraph does not require the presence of any working examples, much less *in vivo* working examples, Applicant has demonstrated a reduction of RSV viral titer in an animal model under the conditions disclosed in the Examples as a result of administration of an ISS without co-administration of an RSV antigen, an immunostimulatory cytokine and an adjuvant.

The Examiner alleges that one skilled in the art would have to determine how to avoid the requirement of antigen in inducing a specific immune response, yet the Examiner acknowledges that it is commonly known that ISS were capable of increasing Th1 activity. Applicants submit that the Examiner has not make a *prima facie* case of non-enablement based on the fact that he believes antigen needs to be co-administered with an ISS in order to induce an immune response. In addition, the claims do not recite "induction of a specific immune response". Claim 1 recites, in part, a method of suppressing a RSV infection.

The Examiner states at page 3 that the claims read on treating RSV infection in any mammal. Claim 1 recites, in part, a method of suppressing a RSV infection in an individual, wherein the individual is a human. The Examiner alleges at page 4 that the specification does not enable using the range of ISS claimed across multiple species. The Examiner *newly* cites Fearon et al., published in 2003, as supporting a Section 112, first paragraph enablement rejection in this 8th Office Action and alleges that structure-function studies show that an ISS that has an immunostimulatory effect in mice may not produce the same effect in humans. With regard to the state of the art, Applicant submits that immunostimulatory polynucleotides are well known in the art and polynucleotides with immunostimulatory sequences active in cells of many mammalian species have been described in scientific literature, including the cells of humans, monkeys, chimpanzees, cows, swine, dogs, cats, rabbits, mice and rats. Fearon et al. acknowledge at page 2114 in the introduction that the *in vivo* activity of ISS ODN as therapeutics in models of asthma and cancer and as vaccine adjuvants has been demonstrated in mice and primates. Fearon et al. further state that while certain oligonucleotides that have optimal immunostimulatory activity in mice can demonstrate relatively little activity in humans, certain other sequences have good activity in both species. The fact that certain ISS may be optimized for use in a mouse model that are not optimum for human use does not in itself support a finding of non-enablement. Applicants respectfully submit that the test for enablement is not whether a certain amount of experimentation is required to practice an invention, but rather whether the amount of experimentation is "undue." As the court held in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988), the test for enablement does not rest merely on the quantity of experimentation that would be required to practice an invention, "since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Applicants have provided disclosure and data in the form of working examples that show how to make and use the claimed invention.

Furthermore, the Examiner at page 6 of the office action acknowledges the potential of the use of *in vitro* assays based on human cell models. The Examiner states that, for example, using the claimed ISS in a whole-cell assay based on human PBMC could be used as a measure of human

efficacy. One of skill in the art would be able to determine ISS that are optimized for human use, although this is not required by the claims, using the assays suggested by the Examiner as being within the knowledge of one of skill in the art.

The Examiner also relies on *newly* cited Marshall et al. published 2005 to support this Section 112, first paragraph enablement rejection of claims in this 8th Office Action and alleges that certain flanking sequences must be present in an ISS to stimulate an immune response. The Examiner alleges that Marshall et al. show that CpG-C sequences which are flanked by a TCG element near the 5' end of the ISS are required for stimulation across multiple species. Applicant points out that the claims do not require stimulation across multiple species. The claims recite, in part, administering a composition to the respiratory track of an individual wherein the individual is a human. Dependent claim 2 recites the sequence 5'-T,C,G-3'. The Examiner alleges at page 4 of the Office Action that the direction of the specification fails to teach one skilled in the art how to use the claimed ISS that lack this element [a TCG element near the 5' end of the ISS]. Applicant disagrees. Applicant invites the Examiner's attention to Examples 1-2 which demonstrate that a ISS, that is, ISS having a sequence as shown in SEQ ID NO:1, which *does not* include a TCG element at the 5' end of the ISS[4] reduced RSV viral titer in the animal model described when administered intranasally. As the Examiner pointed out at page 6 of the Office Action, a whole-cell assay based on human PBMC could be used as a measure of human efficacy for testing of additional ISS that do not contain a TGC element at or near the 5' end of the ISS.

The Examiner at page 6 of the Office Action alleges that the cotton rat examples do not correlate with the invention. Applicant submits as Exhibit B (6 pages), a reference entitled "The Cotton Rat in Biomedical Research" provided by the Animal Welfare Information Center Newsletter dated the Summer 1994, vol. 5, no. 2. This reference states at page 1 that the cotton rat has served as a model for an extensive list of human and rodent pathogens and "currently (that is, at the time of the publication), its use is most important in studies of human RSV".[5] Therefore, contrary to the Examiner's unsupported allegation that the cotton rat examples do not correlate with

[4] SEQ ID NO:1 does have a TCG element toward the 3' end.
[5] Along with other viruses.

the invention, this reference demonstrates that the cotton rat was an accepted animal model for human RSV as early as 1994.

The Examiner at page 7 of the Office Action makes certain allegations regarding Silverman's teachings. The Examiner alleges that Silverman demonstrates that achieving results across species is complicated by a number of variable factors. Applicants submit that Silverman does not stand for the proposition that the Examiner cites it for. Silverman at page 646 states "The effects of ISS-ODN on the immune system depend on the specific sequence, animal species, dose, time, course, and route of delivery, so generalizations must be made with care. For example, the sequence GACGTT activates innate immune cells of the mouse much more efficiently than similar cells from humans. The sequence, GTCGTT confers optimal immunostimulatory effects in human cells". The Silverman statement that "generalizations must be made with care" is unsupported by any citation and in fact the supporting citations that follow in the same paragraph (that is, (9) Krieg et al. and (14) Hartmann et al.) are used by the Examiner to show that CG-containing sequences elicit an immune response in the respective species, even though there may be or, in some cases, may not be, variation in optimal sequences for a particular species. Section 112 first paragraph, enablement, does not require that claims be limited to "optimal" species. Silverman confirms that immunostimulatory effects are elicited by the sequence purine, purine, CG, pyrimidine, pyrimidine. Silverman refers to citations as demonstrating CG sequences that confer immunostimulatory effects in mouse and CG sequences that confer immunostimulatory effects in humans. Nothing in Silverman suggests that any CG sequence does *not* work, only that some CG sequences may be optimized for particular species.

Applicant submits that the specification teaches how to make and use the claimed invention, throughout its scope without undue experimentation. Applicant requests withdrawal of this Section 112, first paragraph enablement rejection of claims. Applicant notes that the previous Section 112, first paragraph written description rejection of claims has been withdrawn.

Rejection of Claims Under 35 U.S.C. §102(e)

Claims 1-4, 6 and 8-14 are rejected under Section 102(e) as allegedly anticipated by Davis U.S. Pat. No. 6,406,705.

Applicants traverse this rejection of claims. In order for a reference to anticipate a claim, each and every element of the claimed invention must be present in the reference. Davis does not teach or disclose the claimed invention and therefore as a matter of law cannot render the claimed invention anticipated. Claim 1 recites a method of suppressing a respiratory syncytial virus (RSV) infection in an individual who has been exposed to RSV, comprising administering a composition to the respiratory tract of said individual, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, wherein RSV antigen, an immunostimulatory cytokine, and an adjuvant are not administered in conjunction with administration of said composition, wherein the individual is a human and wherein said composition is administered in an amount sufficient to suppress an RSV infection. There is no teaching or disclosure in Davis of the claimed invention.

Applicants direct the Examiner's attention to the Davis abstract which states, in part, that the invention relates to adjuvants, and in particular to synergistic *combinations* of immunostimulatory oligonucleotides and non-nucleic acid adjuvants which may be used with an antigen or alone. Davis at col. 2, lines 21-22 states that the invention is useful in one aspect as a method of inducing an *antigen-specific* immune response in a subject. Continuing at col. 2, lines 32-43, Davis states that the combination of the CpG oligonucleotide and the non-nucleic acid adjuvant may be administered with any or all of the administrations of *antigen*. In contrast, the claimed invention recites, in part, that the RSV antigen *is not* administered in conjunction with a composition comprising a polynucleotide comprising an ISS. The presently claimed invention is not rendered anticipated by the disclosures in Davis of methods that comprise administration of an antigen and methods that comprise inducing an antigen-specific immune response by administering an antigen.

In other aspects, Davis discloses the use of *combinations* of two adjuvants, that is a combination of adjuvants wherein the combination includes at least one oligonucleotide containing at least one unmethylated CpG dinucleotide and at least one non-nucleic acid adjuvant. See for example Davis at col. 2, lines 55-67. Davis at col. 2, lines 64-65 discloses that the *combination* of adjuvants is administered simultaneously. Davis at col. 2, lines 65-67 discloses that the *combination* of adjuvants is administered sequentially, that is, one adjuvant may be administered after the other adjuvant *of the combination.* In contrast, the claimed invention recites, in part, that the composition comprising a polynucleotide comprising the ISS *is not administered* with an adjuvant, such as for example, a non-nucleic acid adjuvant. This aspect of Davis that discloses *combinations* of two adjuvants does not render the claimed invention anticipated.

The Examiner alleges at page 8 of the Office Action that the Davis disclosure at col. 2, lines 55-56 "obviously refer to a separate embodiment wherein ISS is not administered with adjuvant or antigen". The Examiner's interpretation of Davis at col. 2, lines 55-56 as referring to "ISS is not administered with adjuvant or antigen" appears contradictory to Davis col. 2, lines 55-62:

> The method includes the step of administering to the subject in order to induce a Th1 immune response a *combination* of adjuvants, wherein the *combination* of adjuvants includes at least one oligonucletide containing at least one unmethylated CpG dinucleotide and at least one non-nucleic acid adjuvant, and wherein the *combination* of adjuvants is administered in an effective amount for inducing a Th1 immune response. (Emphasis added.)

Davis refers to the "combination" of adjuvants 3 times in one sentence at col. 2 lines 55-67, which section the Examiner interprets as "obviously referring to a separate embodiment wherein ISS is not administered with adjuvant or antigen". The Examiner's allegation as to this disclosure of Davis appears to contradict the very teachings of Davis at col. 2, lines 55-67.

The Examiner at page 9 refers to Davis col. 3, lines 3-4, which disclosure is provided below, as anticipating the claimed invention.

> In another aspect, the *same method* is performed but the subject is an infant and the Th1 response can be induced using CpG DNA alone, or CpG DNA in combination with a non-nucleic acid adjuvant at the same or different site, at the same or different time. (Emphasis added.)

This col. 3, lines 3-4 Davis disclosure refers to the *same method*, that is, the method disclosed in this paragraph that continues from col. 2, lines 55-67, which discloses the use of a *combination* of adjuvants (which is in contrast with the claimed invention), which may be administered simultaneously or sequentially. For further explanation, see also Davis col. 15, lines 2-6 which disclose that in cases where the *combination* of adjuvants is given without antigen, with repeated administrations, CpG oligonucleotides or one of the components in the combination may be given alone for one or more of the administrations. The Davis disclosure, col. 3, lines 7-24 disclose a composition comprising a synergistic *combination* of adjuvants (which is in contrast with the claimed invention); col. 3, lines 25-34 which disclose aspects for immunizing an infant which involves the step of administering to an infant an *antigen* (which is in contrast with the claimed invention); col. 3, lines 35-46, which disclose administration of an *antigen* (which is in contrast with the claimed invention); col. 3, lines 47-54, which disclose the administration of *antigen* (which is in contrast with the claimed invention); col. 3, lines 56-67 which disclose the administration of a *combination* of adjuvants (which is in contrast with the claimed invention) wherein at any particular administration, the CpG of the combination may be administered alone at one or more of the administrations.

Assuming *arguendo* that the statement by Davis at col. 3, lines 2-4 does refer to the use of CpG alone for use in an infant to induce a Th1 immune response, which Applicants don't concede because this interpretation would be out of context with i) the Davis disclosure in that very paragraph that discloses *combinations* of adjuvants and 2) with other disclosures in the specification, this statement does not anticipate the claimed invention. Col. 3, lines 2-4 refers to induction of a Th1 immune response in an infant, and does not teach the claimed invention, that is, a method of suppressing a RSV infection in an individual who has been exposed to RSV, comprising administering a composition to the respiratory tract of said individual, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the

ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, wherein RSV antigen, an immunostimulatory cytokine, and an adjuvant are not administered in conjunction with administration of said composition, wherein the individual is a human and wherein said composition is administered in an amount sufficient to suppress an RSV infection.

The Examiner alleges at page 5 of the Office Action that Davis teaches a method for suppressing RSV infection in an individual comprising administering an ISS to the respiratory track of said individual, citing Davis col. 8, lines 56-62; col. 15, line 65; col. 16, line 67; col. 17, line 1 and col. 31, lines 49-60.

Davis col. 8, lines 56-62 disclose:

> In addition to the use of the *combination* of adjuvants for prophylactic treatment, the invention also encompasses the use of the *combination* for the immunotherapeutic treatment of a subject having an infection, an allergy of a cancer. A "subject having an infection" is a subject that has been exposed to an infectious pathogen and has acute or chronic detectable levels of the pathogen in the body". (Emphasis added.)

This Davis disclosure that is directed to the use of *combinations* of adjuvants (which is in contrast to the claimed invention) has no disclosure regarding a method of suppressing a RSV infection in an individual who has been exposed to RSV, comprising administering a composition to the respiratory tract of said individual, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, wherein RSV antigen, an immunostimulatory cytokine, and an adjuvant are not administered in conjunction with administration of said composition, wherein the individual is a human and wherein said composition is administered in an amount sufficient to suppress an RSV infection.

Davis col. 15, line 65 recites "respiratory syncytial virus" and Davis col. 16, line 67-col. 17, line 1 recites "a treatment after the subject (a subject who has been infected) has become infected in order to fight the infection". None of these Davis sections disclose a method of

suppressing a RSV infection in an individual who has been exposed to RSV, comprising administering a composition to the respiratory tract of said individual, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, wherein RSV antigen, an immunostimulatory cytokine, and an adjuvant are not administered in conjunction with administration of said composition, wherein the individual is a human and wherein said composition is administered in an amount sufficient to suppress an RSV infection.

Davis col. 31, lines 49-60 recites

> For use in therapy, an effective amount of the adjuvant *combination* can be administered to a subject by any mode allowing the oligonucleotide to be taken up by the appropriate cells. "Administering" the pharmaceutical composition of the present invention may be accomplished by any means known to the skilled artisan. Preferred routes of administration include but are not limited to oral, transdermal (e.g. via a patch), parenteral injection (subcutaneous, intradermal, intravenous, parenteral, intraperitoneal, intrathecal, etc), or mucosal intranasal, intratracheal, inhalation, and intrarectal, intravaginal, etc). An injection may be in a bolus or a continuous infusion. (Emphasis added.)

Applicants note that this section of Davis relates to administration of the adjuvant *combination* which is in contrast to the claimed invention. This section of Davis cited by the Examiner as supporting the Section 102(e) rejection of claims has no disclosure of the claimed invention, that is, a method of suppressing a RSV infection in an individual who has been exposed to RSV, comprising administering a composition to the respiratory tract of said individual, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, wherein RSV antigen, an immunostimulatory cytokine, and an adjuvant are not administered in conjunction with administration of said composition, wherein the individual is a human and wherein said composition is administered in an amount sufficient to suppress an RSV infection.

The Examiner cites Davis col. 4, lines 18-19, which recites "The oligonucleotide may be any size. Preferably, the oligonucleotide has 8 to 100 nucleotides" as supporting the Section 102(e) rejection of claims. This disclosure of Davis has no teachings of the claimed invention, that is, a method of suppressing a RSV infection in an individual who has been exposed to RSV, comprising administering a composition to the respiratory tract of said individual, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, wherein RSV antigen, an immunostimulatory cytokine, and an adjuvant are not administered in conjunction with administration of said composition, wherein the individual is a human and wherein said composition is administered in an amount sufficient to suppress an RSV infection.

The Examiner at page 5 of the Office Action cites Davis col. 3, lines 4-6 as disclosing "wherein neither a viral antigen nor an immunostimulatory cytokine is co-administered with said ISS". First of all, Davis col. 3, lines 4-6 does not disclose the phrase "wherein neither a viral antigen nor an immunostimulatory cytokine is co-administered with said ISS". Furthermore, the remainder of the paragraph in col. 2 that precedes Davis col. 3, lines 4-6 indicates that this aspect of Davis is within the context of administration of a *combination* of adjuvants, which is in contrast with the claimed invention. This Section of Davis does not disclose the claimed invention.

The Examiner at page 5 also relies upon Davis col. 9, lines 29-32 alleging that it teaches the composition is administered in an amount sufficient to suppress an RSV infection. Davis col. 9, lines 29-32 recites "Thus the *synergistic combination* of adjuvants which induces potent Th1 responses, including CTL, is useful for treating a subject having an infection such as HBV". (Emphasis added.) This section of Davis, which relates to *synergistic combination* of adjuvants is in contrast to the claimed invention, and does not even disclose RSV, much less the claimed invention which is a method of suppressing a RSV infection in an individual who has been exposed to RSV.

The Examiner at page 5 cites Davis col. 30, line 30 and alleges that "Davis further teaches performing its method by administering an ISS having the sequence 5' CACGTTCC-3. Davis at

col. 30, line 30 has no disclosure of the sequence 5' CACGTTCC-3'. Davis SEQ ID NO:42 which appears at col. 30, line 30, does not even include the sequence 5' CACGTTCC-3', much less any disclosure about administering a polynucleotide comprising an ISS (in the respiratory track or otherwise) having this sequence as part of a method for suppressing RSV infection in an individual who has been exposed to RSV.

The Examiner at page 5 cites Davis col. 31, lines 58-60 as teaching administering ISS to the nasal passages and the lungs. Davis col. 31, lines 58-60 recites "or mucosal intranasal, intratracheal, inhalation, and intrarectal, intravaginal etc." This Davis disclosure does not teach the claimed invention, that is, a method of suppressing a RSV infection in an individual who has been exposed to RSV, comprising administering a composition to the respiratory tract of said individual, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-CG-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, wherein RSV antigen, an immunostimulatory cytokine, and an adjuvant are not administered in conjunction with administration of said composition, wherein the individual is a human and wherein said composition is administered in an amount sufficient to suppress an RSV infection.

The Examiner appears to be piecing together sections of Davis disclosure in an attempt to arrive at all the elements of the claimed invention. These separate disclosures of Davis as cited by the Examiner do not, alone or together, teach all the elements of the claimed invention and therefore, cannot by law anticipate the claimed invention. In fact, some of the Davis disclosures cited by the Examiner to support the Section 102(e) rejection of claims are in contrast with the claimed invention. For example, see Davis col. 31, lines 49-60 which recites "For use in therapy, an effective amount of the adjuvant *combination* can be administered to a subject by any mode allowing the oligonucleotide to be taken up by the appropriate cells" and Davis col. 9, lines 29-32 which recites "Thus the *synergistic combination* of adjuvants which induces potent Th1 responses", both of which Davis sections were cited by the Examiner as supporting a Section 102(e) rejection of claims. The claimed invention recites, in part, that RSV antigen, immunostimulatory cytokine, and

an adjuvant *are not* administered in conjunction with administration of said composition (comprising a polynucleotide comprising an ISS). Thus, these examples of Davis disclosures relied upon by the Examiner are in contrast to the claimed invention. Even if all the elements of the claimed invention were present Davis, Davis is not enabled for the instant claimed invention,

The Examiner at page 5 of the Office Action alleges that regarding claim 10, "suppression comprises a reduction of RSV titer in a biological sample from said individual" is inherent to the teachings of Davis. Davis does not disclose all the elements of the claimed invention; and instant claim 10 does not necessarily flow from the teachings of Davis. In fact, RSV is only mentioned among a larger listing of numerous viruses; there are no specific teachings regarding RSV in Davis.

Thus, Davis does not teach or disclose all the elements of the claimed invention. Since Davis does not teach each and every element of the claimed invention, the reference cannot by law anticipate the claimed invention. Applicant requests withdrawal of this rejection of claims.

Rejection of Claims Under 35 U.S.C. §103(a)

Claims 11-14 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Davis.

Applicants traverse this Section 103 rejection of claims. To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Also, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20USPQ2d 1438 (Fed. Cir. 1991); MPEP §2143.

Claims 11-14 are directed to a kit for use in the method of the invention comprising a composition comprising an ISS-containing polynucleotide and instruction for administration of the

composition to the respiratory tract of an individual. The polynucleotide is greater than six and less than about 200 nucleotides in length and the ISS comprises the sequence 5'-CG-3'.

Davis is discussed above. Those arguments are reiterated here. Additionally, Davis does not teach or suggest producing a kit as claimed, which the Examiner concedes in the Office Action at the paragraph bridging pages 5-6. Thus, Davis provides no teaching or suggestion of the claimed invention. Further, Applicant respectfully submits that there is no suggestion or motivation in Davis to modify the teachings therein to arrive at the claimed invention.

Thus, Applicant respectfully submits that a *prima facie* case of obviousness has not been established with regard to claims 11-14.

Without acquiescing to this rejection and solely in an interest to expedite prosecution, Applicant has canceled claims 11-14 thereby obviating this rejection of claims.

Applicant respectfully requests that this rejection be withdrawn.

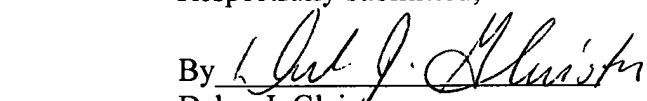
CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882000900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: March 20, 2006

Respectfully submitted,

By 

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